

The opinion in support of the decision being entered today
is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte PAUL P. LATTA

Appeal 2007-1152
Application 10/660,924
Technology Center 1600

Decided: October 10, 2007

Before ERIC GRIMES, LORA M. GREEN, and RICHARD M.
LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the Examiner's final rejection of claims 2-9. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

The Specification describes methods of creating immunological tolerance to cells and tissues comprising implanting in the mammal a tolerizing dose of cells or tissue encapsulated in a biologically compatible permselective membrane (Spec. 3). The Specification states that this

process can be used to prevent certain diseases, such as Type I diabetes (Spec. 10: 12-17).

Claims 2-9 are pending and appealed (Supp. Appeal Br.¹ 2). Claims 2-9 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement (Answer 4) and also for lacking written description (Answer 8).

We select claim 2, the only independent claim on appeal, as representative of the claims. It reads as follows:

2. A method of preventing onset of Type I diabetes in a mammal predisposed to Type I diabetes, comprising implanting a dose of insulin-producing cells encapsulated in a biologically-compatible membrane into an implantation site in said mammal prior to onset of Type I diabetes, wherein said dose is at least one order of magnitude less than that necessary to achieve normoglycemia in a mammal of the same species.

DISCUSSION

Enablement rejection

“To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). “When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the

¹ “Supp. Appeal Br.” is a reference to the Supplemental Appeal Brief which is date stamped Jul. 19, 2006.

specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. . . . *Marzocchi*, 439 F.2d at 223-24, 169 USPQ at 369-70.” *In re Wright*, 999 F.2d at 1561-62, 27 USPQ2d at 1513 (Fed. Cir. 1993).

Enablement is determined as of the application filing date. *See In re Brana*, 51 F.3d 1560, 1567 n.19, 34 USPQ2d 1436, 1441 n.19 (Fed. Cir. 1995). Thus, the issue in this rejection is whether the Examiner has set forth a reasonable explanation as to why the scope of protection provided by the claims is not adequately enabled by the Specification as of the application filing date.

The Examiner contends that the Specification does not adequately teach how to effectively prevent the onset of Type I diabetes in any mammal predisposed to it (Answer 4). The Examiner asserts that the Specification “only discloses the effects of the implanting of insulin-producing cells on the level of blood glucose using streptozotocin-induced [diabetes] in murine experimental model, using NOD mouse. (See Examples 1-2 in particular)” (Answer 4). However, the Examiner contends that the examples are insufficient to enable the scope of the claims because “the state of the art is that it is unpredictable [from] the in vivo murine data using NOD model disclosed in the specification as [to] whether the instant invention can be used for the in vivo preventing onset of type I diabetes in mammals including human” (Answer 7). To support the position that the murine model is not adequate to predict the efficacy of the method as it is broadly claimed, the Examiner cites six literature references: Atkinson (*Nature*, 1999, vol. 5, pages 601-604), Knip (*Acta Paediatr. Suppl.*, 1998, vol. 452, pages 54-62), Metas (*J. of Immunology*, 2004, vol. 172, pages 2731-2738),

Tufveson (*Immun. Reviews*, 1993, No. 136, pages 101-107), Feldman (*Transplant. Proc.*, 1998, vol. 30, pages 4126-4127), and Cochlovius (*Modern Drug Discovery*, October 2003, pages 33-38), and discusses their relevance to the enablement issue (Answer 4-7).

We have considered the Examiner's arguments and the supporting documents, but do not find that the evidence is sufficient to sustain the rejection.

In beginning our analysis, we note that the Examiner did not correctly characterize the disclosure in the Specification. Example 1 describes the treatment of streptozotocin-induced diabetes in C57B6 mice (Spec. 19: 30 to 20: 3), not NOD mice as stated on page 4 of the Answer. The Specification provides experimental evidence in this example that a tolerizing first dose of encapsulated insulin-producing cells induced immunological tolerance to a subsequent curative dose of cells.

Turning to the references cited by the Examiner in support of his position, we first address Mestas (*supra*.). The Examiner states that Mestas provides evidence of the inadequacy of mouse models in predicting the efficacy of therapies for human disease (Answer 5). Mestas – as noted by the Examiner – describes the differences between mouse and human immunology, concluding that “[s]uch differences should be taken into account when using mice as preclinical models of human disease” (Mestas, Abstract). Mestas describes its purpose as “to understand the potential limitations of extrapolating data from mice to humans” (Mestas, at 2731, col. 2). After extensively characterizing the immunological differences, Mestas concludes:

While caution in interpreting preclinical data obtained in mice is clearly warranted, we believe that with these caveats in mind, mice will continue to be the premiere *in vivo* model for human immunology and will be absolutely essential for continued progress in our understanding of immune function in health and disease.

(Mestas, at 2736, col. 2.) Thus, far from abandoning the mouse as a model of human disease, Mestas characterizes it as “absolutely essential for continued progress” in understanding immunological diseases.

The Examiner contends that Tufveson’s statement that “today’s small animal models seem to be insufficient to produce data for clinical decision-making” (Tufveson, at 101) raises reasonable doubt about the predictability of mouse models (Answer 6). However, Tufveson concluded that after “this airing of problems in the clinical field it is clear that small animal models are sought” for human disease (Tufveson, at 101). Tufveson reviewed its own efforts at developing such models and concludes that “it would seem to be reasonable to test new immunosuppressive drugs . . . in allograft models” (Tufveson, at 107). Thus, Tufveson does not disavow the use of animal models nor does it provide any evidence that the particular mouse model described in the Specification is deficient.

With respect to the NOD mouse model of Type I diabetes, Atkinson acknowledges that “specific differences . . . restrict their interpretation” (Atkinson, at 601, col. 2), but also states that “investigations of NOD mice have enhanced our appreciation of the etiologic complexity of type I diabetes in humans and provided an example of how promising results obtained in an animal model can be translated into human clinical trials” (Atkinson, at 604, col. 1). Thus, contrary to the Examiner’s position,

Atkinson recognizes that NOD mice – despite species differences – have value in predicting outcome in human disease.

Appellant provided two declarations by Dr. David Scharp (“Declaration of David Scharp, M.D.”, dated Nov. 25, 2003, and “Second Declaration of David Scharp, M.D. under 37 C.F.R. § 1.132”, dated Apr. 28, 2005) showing that NOD mice who received the treatment described in the Specification were prevented from becoming diabetic (Supp. Appeal Br. 5-6; Declaration of David Scharp, M.D., ¶ 5-8). For example, Scharp showed that 3 out 10 mice who received the tolerizing dose of encapsulated islet cells, prior to the onset of diabetes, remained diabetes-free after eight weeks (Declaration of David Scharp, M.D., ¶ 10). Atkinson states that NOD mouse are the favored model for Type I diabetes (Atkinson, at 601, col. 1), and as discussed above, considered them an important tool for understanding and developing treatments for diabetes (Atkinson, at 604, col. 1).² Thus, we find the post-filing evidence in the Scharp Declarations sufficient “to prove that the disclosure was in fact enabling when filed.” *In re Brana*, 51 F.3d 1560, 1576, fn.19, 34 USPQ2d 1436, fn.19 (Fed. Cir. 1995).

The Examiner’s position appears to be that because mouse models don’t always work,³ they cannot be relied upon to enable a specification –

² Dr. Scharp makes similar comments about the value of NOD mice, including their proven value in developing markers for predicting human patients who will develop clinical Type I diabetes (Second Declaration of David Scharp, M.D. under 37 C.F.R. § 1.132, ¶ 2).

³ “Mestas . . . teach that there exist significant differences between mice and humans in immune system development . . . [quoting Mestas:] [‘]As therapies for human diseases become ever more sophisticated and specifically targeted[,] it becomes increasing important to understand the *potential limitations of extrapolating data* from mice to humans. *The*

there being always a degree of uncertainty about whether the treatment will prove to be effective in humans. In our opinion, this is not a reasonable standard by which to measure enablement.

The publications cited by the Examiner acknowledge that there are weaknesses in available mouse models as surrogates for human disease, but these same publications continue to use the animal models to study human disease because the animal models are apparently “‘as good as it gets’, short of a study in humans” (Atkinson, at 601).

In cases where the utility of claimed compounds were questioned, the Federal Circuit has repeatedly held that in vitro and animal tests, when reasonably correlated with the in vivo activity asserted as the utility, were sufficient to satisfy the utility requirement of 35 U.S.C. § 101. *Cross v. Iizuka*, 753 F.2d 1040, 1051, 224 USPQ 739, 747 (Fed. Cir. 1985). In *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), the PTO had argued that mouse data was insufficient to establish utility for a cancer treatment drug. In rejecting this position, the Federal Circuit wrote:

The Commissioner counters that such in vivo tests in animals are only preclinical tests to determine whether a compound is suitable for processing in the second stage of testing, by which he apparently means in vivo testing in humans, and therefore are not reasonably predictive of the success of the claimed compounds for treating cancer in humans. The Commissioner, as did the Board, confuses the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption. *See Scott v. Finney*, 34 F.3d 1058, 1063, 32

literature is littered with the examples of therapies that work well in mice but fail to provide similar efficacy in humans[’] [Mestas, at 271] (emphasis added)” (Answer 5).

USPQ2d 1115, 1120 (Fed. Cir. 1994) (“Testing for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings.”). (*Brana*, at 1567, 34 USPQ2d at 1442.) We see no reason why enablement of a method claim whose scope includes humans should likewise require human testing. Thus, in view of *Brana*, we conclude that animal models can be used to establish enablement under § 112, first paragraph of a method claim.

The relevant standard is rather whether the scope of the claims bears “a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.” *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). *See also Invitrogen Corp. v. Clontech Laboratories Inc.*, 429 F.3d 1052, 1071, 77 USPQ2d 1161, 1173-1174 (Fed. Cir. 2005). In this case where an animal model serves as the enablement for the claimed method, the proper question is whether it reasonably correlates with the method for which patent protection is sought. On this point, the Examiner has provided no evidence that results obtained with streptozotocin-induced diabetes in C57B6 mice, as described in the Specification, do not reasonably correlate with the scope of claim 2. In contrast, Appellant has provided post-filing evidence, that together with Atkinson’s teaching about the acceptability of NOD mouse as a model for diabetes, establishes by the preponderance of the evidence that the Specification as filed is, in fact, enabling. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) (“[P]atentability is determined on the totality of the record, by a preponderance of the evidence.”).

The Examiner has provided no other explanation as to why the claim is not adequately enabled for the claimed method of preventing onset of Type I diabetes. Thus, on the record before us, we conclude that the Examiner has not sustained the burden of establishing a reasonable basis to question the scope of enablement of the claimed invention. We reverse the rejection of claims 2-9 for lack of enablement

Written description rejection

Under 35 U.S.C. § 112, first paragraph, the specification must contain a written description of the invention. Thus, when claims are amended during patent prosecution, the claimed invention, in its amended form, must be described in the specification. “An applicant complies with the written description requirement ‘by describing the invention, with all its claimed limitations.’ *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997).” *Gentry Gallery v. The Berkline Corp.*, 134 F.3d 1473, 1479, 45 USPQ2d 1498, 1502-1503 (Fed. Cir. 1998).

The Examiner contends that claims 2-9, which were added by an amendment dated April 1, 2004, are not described in the Specification as it was originally filed (Answer 8). The Examiner argues that the Specification “as originally filed only disclosed [a] two-step process” involving tolerizing and curative doses (Answer 12), not a one-step method of “preventing type I diabetes comprising … implanting a tolerizing dose of insulin-secreting cells” in which the dose is at least one order of magnitude less than a curative dose (Answer 12). We do not agree.

The Specification in its original disclosure describes a one-step process of administering a tolerizing dose of insulin-secreting cells. In the “Summary of the Invention,” it is stated:

One embodiment of the invention is a method of creating immunological tolerance to foreign cells, tissues or organs in a mammal, comprising the step of implanting in the mammal a tolerizing dose of foreign cells or tissue encapsulated in a biologically compatible permselective membrane. The method may additionally comprise the step of administering to the mammal a curative dose.

(Spec. 3-4.)

An original claim of the Specification also describes a single step method:

1. A method of creating immunological tolerance to foreign cells, tissues or organs in a mammal, comprising the step of implanting in said mammal a tolerizing dose of corresponding foreign cells or tissue which shed antigens contained in or on said foreign cells [,] tissues or organs, said corresponding foreign cells or tissue being encapsulated in a biologically-compatible permselective membrane.

(Spec. 27.)

The tolerizing dose is characterized in the original Specification as being “one to two orders of magnitude less than the curative dose” (Spec. 4: 26-27) and “one or two orders of magnitude less than a full dose implant” (Spec. 12: 26-27). It is stated in the Specification that the “amount of cells . . . necessary for the initial tolerizing implant will vary” (Spec. 12: 24-25) and “the size of these doses . . . can be optimized” (Spec 12: 30-31). Thus, the Specification describes a dose of one order of magnitude less than a curative dose (i.e., the dose recited in claim 2 which is “necessary to achieve normoglycemia in a mammal of the same species”) and that this amount

could be routinely varied. Thus, we conclude that the limitation “wherein said dose is at least one order of magnitude less than that necessary to achieve normoglycemia in a mammal of the same species” is supported by the originally filed Specification.

The Specification also explicitly describes preventing diabetes using a single dose of cells – the method of instant claim 2:

The process of the invention can also be used to prevent certain diseases, particularly autoimmune disorders. In these cases the process is as follows. First, patients at high risk for the disease or already in the very early phase of the disease are identified. At the critical time of the onset, the process is intervened with the small encapsulated tissue. For example, islets are used for Type I diabetes and collagen is used for arthritis. This implant of foreign tissue immediately diverts the attention of the immune system to the new foreign invader and it begins the process to destroy this new threat. Because of this diversion, the process of self-destruction of desirable tissue that was just beginning is suppressed, then abandoned, then forgotten. It is, in essence, “switched off” and the damage is prevented.

(Spec. 10: 12-21.) It is also stated that implants for prevention of disease can be in tolerizing amounts (Spec 19: 1-15).

In sum, we find that all the limitations of claim 2 are described in the originally filed Specification. Accordingly, the rejection of claims 2-9 as lacking written description is reversed.

CONCLUSION

The rejection of claims 2-9 under 35 U.S.C. § 112, first paragraph, as lacking enablement and written description are

REVERSED.

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE CA 92614